

REMARKS

The specification has been amended to correct grammatical errors discovered by Attorneys for Applicants during review of the application.

Claims 1, 4-34, 36, 45, 46, 86-90, 157-181, 183, 212, 213, 263-267 and 280-292 were pending in the application. In the Office Action mailed March 22 2004, claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265 and 280-292 are rejected (claims 46, 88, 212-213 and 266-267 having been withdrawn from consideration as drawn to non-elected species). In the instant Amendment, claims 1, 10, 36, 157, 183, 263-264 and 284-285 have been amended, and new claims 293-296 have been added. Upon entry of the above-made amendment, claims 1, 4-34, 36, 45, 46, 86-90, 157-181, 183, 212, 213, 263-267 and 280-296 will be pending.

Claim 1 has been amended to clarify that in the claimed method in which at least one gene in the plurality of different genes has an exon having a plurality of different variants, the step of measuring comprises measuring the expression level of each of the plurality of different variants of the exon in the gene. Support for the amendment is found in the specification at, e.g., page 9, lines 21-29; page 20, lines 19-33; page 38, lines 10-26; and FIG. 1. For example, as discussed on page 9, lines 21-29, of the specification, FIG. 1 is an illustration of a gene having several exons, exons 1-4. In FIG. 1, exon 3 (103) and exon 4 (104) each has several different variants. FIG. 1 also illustrates probes that can be used for measuring the expression level of these variants. The disclosures on page 20, lines 19-33, and page 38, lines 10-26, describe the claimed method in detail.

Claim 1 has also been amended to clarify that each of the plurality of different variants is a different splice form of the exon generated using a different 3' or 5' splice junction of said exon. Claims 284 and 285 have been amended similarly. Support for the amendment is found in the specification at page 9, lines 21-29; page 13, lines 20-22; and FIG. 1. The cited disclosure specifically states that a variant of an exon is a particular splice form of the exon, e.g., a splice form generated using one of several possible 5' or 3' splice junctions. Using exon 3 of FIG. 1 as an illustration, a variant can be a splice form of the exon generated using the common 5' splice junction and one of the three possible 3' junctions.

Claims 10 and 157 have been amended to include the recitation that the plurality of probes comprises probes that allow measurement of the expression levels of the plurality of different variants of the exon. Support for the amendment is found in the specification at page 20, lines 20-33; and page 38, lines 10-26. For example, the disclosure at page 38, lines 10-26, describes that measurement of the expression levels of the plurality of different variants of the exon can be achieved using probes, such as a set probes of successive overlapping sequences or a set of probes comprising exon specific probes and/or variant junction probes.

Claims 36 and 183 have been amended to recite that the expression levels are measured as abundance *of mRNA transcripts* (emphasis added). Support for the amendment is found in the specification at page 11, lines 28-32. The cited section of the disclosure recites that the expression level of an exon refers to the abundance of mRNA transcripts containing the exon.

Claim 263 has been amended to recite that the successive overlapping probes tile along the longest *length* variant among said plurality of different variants of said exon (emphasis added). Support for the amendment is found in the specification at page 13, lines 22-27; page 20, lines 24-28; and page 38, lines 7-15; and FIG. 1. For example, the disclosure at page 38, lines 10-12, describes that a set of successive overlapping sequences tiled across the genomic region containing the longest variant of an exon can be included in the exon profiling array. In FIG. 1, such a set of probes is illustrated for exon 3 (103).

Claims 264 and 284-285 have been amended to replace the word “neighboring” with the word “adjacent.” Support for the amendment is found in the specification at page 13, lines 28-30, and page 38, lines 18-22. The cited sections of the specification demonstrate the usage of the word “neighboring” in the present application, i.e., the term “neighboring exons” refers to exons that are next to or adjacent to each other in an mRNA. See also page 13, lines 28-30, of the specification for such usage.

Claims 284-285 have been amended to recite “one or more exon specific probes *comprising* different nucleotide sequences for each of a plurality of different genes in the genome of said organism” (emphasis added). Support for the amendment is found in the specification at page 37, lines 33-35; page 38, lines 10-25; and FIG. 1.

New claims 293-296 have been added. Support for these new claims is found in the specification at page 13, lines 17-22. The cited section specifically describes that at least ... 5, 10, ..., 100, ..., 1,000, ..., different expressed variants of exons may be determined in determination of exon expression state.

No new matter has been added by these amendments. Entry of the foregoing amendments and consideration of the following remarks are respectfully requested.

APPLICANTS' INTERVIEW SUMMARY

Applicants thank Examiner Frank Lu, Ph.D., for the courtesies extended during the telephone interview on August 16, 2004 (hereinafter "the Interview") with Adriane M. Antler, Ph.D., R. Douglas Bradley, Ph.D., and Weining Wang, Ph.D. During the interview, the objection and rejections in the Office Action mailed March 22, 2004 were discussed. Claim rejection under 35 U.S.C. § 112, second paragraph, was then discussed. Proposed claim amendments were also discussed.

With respect to the Examiner's objection in paragraph 2 of page 2 of the Office Action, Dr. Antler pointed out that in the Amendment filed on November 5, 2003, Applicants did not file a substitute specification. Dr. Antler also pointed out that there is a Figure 4c in the formal drawings. The Examiner acknowledged that such was indeed the case.

With respect to the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, stated in paragraph 5 of the Office Action, Dr. Antler proposed to amend the claim to recite that at least one gene in said plurality of different genes has an exon having a plurality of different variants. The Examiner indicated that such an amendment would overcome the rejection.

With respect to the rejection of claim 1 under 35 U.S.C. § 112, second paragraph, stated in paragraph 6 of the Office Action, Dr. Antler explained that the first part of the claim requires measuring the expression levels of a plurality of different individual exons or different individual multiexons in each of a plurality of different genes, whereas the second part of the claim requires that, among the plurality of different individual exons or multiexons in each of a plurality of different genes measured in the first part of the claim, at least one gene has an exon that has a plurality of different variants, and that the claimed method comprises measuring the expression level of each of the plurality of different variants of the

exon. The Examiner indicated that explaining such in Applicants' response should overcome the rejection.

With respect to the rejection of claim 1 and claims 284 and 285 under 35 U.S.C. § 112, second paragraph, stated respectively in paragraphs 7 and 14 of the Office Action, Dr. Antler explained that, as illustrated in FIG. 1 of the application and the accompanying text (see page 9, lines 21-29 of the specification), variants of an exon (e.g., exon 103 and exon 104 in FIG. 1) share either a 5' or 3' end and differ in a 3' or 5' end. Dr. Antler proposed to amend the claim to recite that the variants of an exon are different splice forms of the exon (emphasis added). The Examiner indicated that such an amendment would overcome the rejection.

With respect to the rejection of claims 10 and 157 under 35 U.S.C. § 112, second paragraph, stated respectively in paragraphs 8 and 10 of the Office Action, Dr. Antler proposed to amend the claims to recite that "said plurality of probes comprises probes that allow measurement of the expression levels of said plurality of different variants of said exon." The Examiner indicated that the amendment would overcome the rejection.

With respect to the rejection of claims 36 and 183 under 35 U.S.C. § 112, second paragraph, stated in paragraph 9 of the Office Action, Dr. Antler proposed to amend the claims to recite that said expression levels are measured as abundance of mRNA transcripts (emphasis added). The Examiner indicated that such an amendment would overcome the rejection.

With respect to the rejection of claim 263 under 35 U.S.C. § 112, second paragraph, stated in paragraph 11 of the Office Action, the Examiner suggested that Applicants amend the claim to make it clear that the longest variant refers to the variant that has the longest length, in order to obviate the rejection. Dr. Antler agreed to make the amendment according to the suggestion of the Examiner.

With respect to the rejection of claim 264 and claims 284 and 285 under 35 U.S.C. § 112, second paragraph, stated respectively in paragraphs 12 and 15 of the Office Action, the Examiner suggested that Applicants amend the claims to recite "adjacent" instead of "neighboring," in order to obviate the rejection. Dr. Antler agreed to make the amendment according to the suggestion of the Examiner.

With respect to the rejection of claim 284 under 35 U.S.C. § 112, second paragraph, stated in paragraph 13 of the Office Action, Dr. Antler proposed to amend the claim to recite one or more exon specific probes comprising different nucleotide sequences (emphasis added). The Examiner indicated that he wished to re-review the rejection, but that the amendment would overcome the rejection.

NO SUBSTITUTE SPECIFICATION WAS FILED ON NOVEMBER 5, 2003

In the Office Action mailed March 22, 2004, the Examiner indicates that the “substitute specification filed on November 5, 2003 has not been entered.” The Examiner contends that the “substitute specification” does not conform to 37 C.F.R. 1.125(b) and (c) because a clean copy of the substitute specification was not supplied. Applicants respectfully point out that the amendments to the specification as filed on November 5, 2003 were made in the manner of “adding, deleting, or replacing paragraph” according to Revised 37 C.F.R. 1.121(b)(1) rather than in the manner of a substitute specification according to Revised 37 C.F.R. 1.121(b)(3), and were made in full conformity with the Revised 37 C.F.R. 1.121(b)(1).

The Examiner also contends that there is no Figure 4c in the drawings. Applicants respectfully point out that although the informal drawings do not contain a Figure 4c, the formal drawings filed April 1, 2003 *do* contain a Figure 4c. Indeed, the Examiner objected to the disclosure for the lack of a description of Figure 4c in the Office Action mailed July 1, 2003.

Therefore, the Examiner’s objections should be withdrawn.

THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, SHOULD BE WITHDRAWN

Claims 1, 4-34, 36, 45, 86, 87, 89, 90, 157-181, 183, 263-265 and 280-292 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In paragraph 5 of the Office Action, claim 1 is rejected because there is no recitation that an exon in at least one gene has a plurality of variants before the phrase “measuring the expression level of each of a plurality of different variants of an exon in said at least one

gene.” Applicants have amended claim 1 to add such a recitation. The rejection is therefore obviated and should be withdrawn.

In paragraph 6 of the Office Action, claim 1 is rejected as being vague and indefinite. The Examiner contends that the first part of the claim, which recites measuring the expression levels of a plurality of different individual exons or different individual multiexons, and the second part of the claim, which recites measuring the expression level of each of a plurality of different variants of an exon in said at least one gene, do not correspond to each other. As discussed during the Interview, the second part of the claim further limits the first part of the claim by requiring that, among the plurality of different individual exons or multiexons measured in the first part of the claim, at least one gene has an exon that has a plurality of different variants, and the claimed method comprises measuring the expression level of each of these variants. The rejection should therefore be withdrawn.

In paragraphs 7 and 14 of the Office Action, claim 1 and claims 284-285 are respectively rejected as being unclear what the phrase “each of said plurality of different variants being a form of said exon” means. Applicants have amended the claims to recite that each of said plurality of different variants is “a different splice form of said exon.” The rejection is therefore obviated and should be withdrawn.

In paragraphs 8 and 10 of the Office Action, claims 10 and 157 are respectively rejected under 35 U.S.C. § 112, second paragraph, as being vague and indefinite. The Examiner contends that the array respectively recited in claim 10 and 157 does not contain probes that can detect the plurality of variants. Applicants have amended the claim to include the recitation that “said plurality of probes comprises probes that allow measurement of the expression levels of said plurality of different variants of said exon.” The rejection is therefore obviated and should be withdrawn.

In paragraph 9 of the Office Action, claims 36 and 183 are rejected as being unclear regarding what kind of expression level can be considered as “abundance.” Applicants have amended the claims to recite that “said expression levels are measured as abundance of mRNA transcripts” (emphasis added). The rejection is therefore obviated and should be withdrawn.

In paragraph 11 of the Office Action, claim 263 is rejected as being unclear regarding the meaning of the phrase “the longest variant of an exon.” Applicants have amended the claim to recite that the successive overlapping probes tile along the “longest length variant” among said plurality of different variants of said exon. The rejection is therefore obviated and should be withdrawn.

In paragraphs 12 and 15 of the Office Action, claim 264 and claims 284-285 are respectively rejected as being unclear regarding the meaning of the phrase “a sequence spanning the splice junction between a different variant of said exon having a plurality of different variants and a neighboring exon.” Applicants have amended the claim to replace “neighboring” with “adjacent.” The rejection is therefore obviated and should be withdrawn.

In paragraph 13 of the Office Action, claim 284 is rejected as being unclear regarding the meaning of the phrase “one or more exon specific probes of different nucleotide sequences for each of a plurality of different genes in the genome of said organism.” Applicants have amended the claim to recite “one or more exon specific probes comprising different nucleotide sequences for each of a plurality of different genes in the genome of said organism.” The rejection is therefore obviated and should be withdrawn.

CLAIMS WITHDRAWN FROM CONSIDERATION AS BELONGING TO NON-ELECTED SPECIES SHOULD BE CONSIDERED


Claims 46, 88, 212, 213, 266 and 267 were withdrawn from consideration by the Examiner as belonging to non-elected species. Since Applicants believe that the generic claims are allowable, claims 46, 88, 212, 213, 266 and 267 should be considered by the Examiner. Applicants respectfully request that these claims be considered by the Examiner.

CONCLUSION

Applicants respectfully request entry of the foregoing amendments and remarks into the file of the above-identified application. Applicants believe that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and allowance of the application are respectfully requested.

Respectfully submitted,

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Adriane M. Antler 32,605
JONES DAY (Reg. No.)
222 East 41st Street
New York, New York 10017-6702
Phone: (212) 326-3939